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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/591,172	04/26/2007	Mitsuo Sekine	4600-0129PUS1	6068

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EXAMINER	
CRANE, LAWRENCE E	

ART UNIT	PAPER NUMBER
1623	

NOTIFICATION DATE	DELIVERY MODE
04/03/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/591,172	SEKINE ET AL.	
	Examiner	Art Unit	
	Lawrence E. Crane	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *Auust 30, 2006 (preliminary amendment)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-10 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-10 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/14/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The Abstract of the Disclosure is objected to because is does not meet the requirement of the MPEP for US application. Correction is required. See MPEP 608.01(b).

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts, compounds or compositions, the general nature of the compound or composition should be given as well as its use, e.g., "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary. Complete revision of the content of the abstract is required on a separate sheet.

Applicant is respectfully requested to amend the abstract because the present abstract does not describe the proposed amendment with an emphasis on how applicant's process represents a change from prior art processes for oligonucleotide synthesis.

The instant disclosure fails to include "Cross-References to Related Applications." See 37 C.F.R. §1.78 and MPEP at §201.11. Applicant is respectfully requested to include the requested information as the first paragraph of the disclosure.

Claims **1 and 11-13** have been cancelled, claims **2-4, 7, 9, 10 and 14** have been amended, the disclosure has been amended at several locations in re sequence information, and no new claims have been added as per the preliminary amendments filed August 30, 2006 and August 13, 2007. One Information Disclosure Statement (1 IDS) filed December 14, 2006 has been received with copies of all cited references non-US Patent references and made of record. An oligonucleotide Sequence Disclosure and CFRE have been filed, reviewed, and found acceptable.

Claims **2-10 and 14** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line y, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

35 U.S.C. §101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title."

Claims **2, 9, 10 and 14** are rejected under 35 U.S.C. §101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. §101. See for example *Ex parte Dunki,* 153 USPQ 678 (Bd. App., 1967) and *Clinical Products, Ltd. v. Brenner,* 255 F. Supp. 131, 149, 149 USPQ 475 (D.D.C. 1966).

Claims **2-10 and 14** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for the synthesis of oligonucleotides via phosphoramidite intermediates wherein the monomeric intermediates have no base amino group protection, does not reasonably provide enablement for any synthesis wherein protection is present, an alternative not excluded by claim **2**. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims is found to be excessive because the instant claims do not completely exclude the possibility of N-protected bases being intermediates in the process, while the instant disclosed embodiments require that there are no heterobase amino group protecting substituents. In addition, the term "alcohol-type" compound is too broad because the specific exemplifications rely only on phenolic compounds or an N-hydroxybenzotriazole for this role, in the presence of an activator that is an imidazole or a tetrazole.

B. The nature of the invention is directed to the synthesis of oligonucleotides via phosphoramidite intermediates wherein there are no N-heterobase amino protecting substituents, and consequently no need to apply a deprotection step to remove same. This is accomplished by reacting the phosphoramidite intermediates with the free hydroxyl groups of

the growing oligonucleotide chain in the presence of an phenolic or N-hydroxybenzotriazole catalytic compound

C. The state of the prior art: The prior art does disclose previous attempts to make oligonucleotides wherein there are no amino protecting groups on the heterobase substituents, but these methods differ from the instant process because they do not rely on a phenolic or N-hydroxybenzotriazole catalyst.

D. The level of one of ordinary skill: One of ordinary skill would be expected to be familair with the automated synthesis of oligonucleotides, and the chemistry of the phosphoramidite reagents and the products typically generated by this process.

E. The level of predictability in the art: This area of oligonucleotide synthesis is fairly new and therefore not very predictable in view of the small number of attempts that have been applied successfully to avoid the presence of N-amino protecting groups.

F. The amount of direction provided by the inventor: This subject is dealt with in a previous paragraph.

G. The existence of working examples: This subject is dealt with in a previous paragraph.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is found to be excessive because the instant claims have failed to reasonably limit the claimed subject matter to the invention enabled herein. .

Claims **2-4, 7, 9 and 14** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **2** the term "alcohol-type compound" is incomplete because said term fails to completely and accurately describe the compounds required as catalysts for the claimed process to be executed.

In claim **2** the term "acid catalyst as an activator" is generic to a vast array of compounds most of which are not applicable as catalyst for the instant claimed process; e.g. sulfuric acid,

etc., etc. For this term to accurately describe the process, a listing of appropriate compounds that are actually activators should be added to the claim by amendment.

In claim **3** the terms "HOBt-derivative" and "phenol analogue" are both indefinite for failure to define the metes and bounds of the included terms "derivative" and :"analogue." See also claims **4 and 7** wherein similar errors occur.

In claim **9** the term "wherein a mixture comprising an equal amount of ... is used as the activator" is inconsistent with previous definition of the term "activator." Appropriate amendment to address this inconsistent application of terminology is respectfully requested. See also claim **14** wherein a similar error occurs.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent."

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

(e) the invention was described in

(1) an application for patent described under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application filed under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a)."

(f) he did not himself invent the subject matter sought to be patented."

Claims **2-10 and 14** are rejected under 35 U.S.C. §102**(a)** as being anticipated by **Sekine et al. '532** (PTO-1449 ref. **BA**).

THe instant claims are anticipated by the instant disclosed process, a process that is applicant's own work in the form of an earlier published Japanese patent application.

Claims **2-10 and 14** are rejected under 35 U.S.C. §102(**a**) as being anticipated by **Ohkubo et al.** (PTO-1449 ref. **CA**).

THe instant claims are anticipated by the instant disclosed process, a process that is applicant's own work in the form of an earlier published journal article.

Claims **2, 3, 6, 7, 9 and 10** are rejected under 35 U.S.C. §102(**b**) as being anticipated by **Dabkowski et al.** (PTO-1449 ref. **CB**).

The instant disclosed process of **Dabkowski et al.** in its abstract discloses that there is no need for an activator when 2,4-dinitrophenol is present in a phosphoramidite-type oligonucleotide synthesis coupling process. This disclosure renders the instant claims anticipated because the addition of a unnecessary activator as specified herein is not required to achieve the expected result. Therefore, the instant claimed process is not distinguishable from the cited prior art, and is therefore anticipated thereby.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. §1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §§102(f) or (g) prior art under 35 U.S.C. §103(a).

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < http://pair-direct.uspto.gov >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

LECrane:lec
03/29/2009

/Lawrence E. Crane/

Primary Examiner, Art Unit 1623

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